A century of NAD+ insights drives aging science and solutions innovations

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Dr. Rebecca Crews from Renue By Science, LLC, outlines a century of NAD+ insights driving aging science and, innovative solutions and much more

Nicotinamide adenine dinucleotide. NAD+ is essential for human health and is central to cellular metabolism, DNA repair, and many other essential operations. Over a century ago, its importance became clear when a deficiency in niacin, a precursor to NAD+, was linked to pellagra – a devastating disease characterized by dermatitis, diarrhea, dementia, and death. The diverse and severe symptoms of pellagra underscored just how crucial NAD+ is to the body's basic functions.

This discovery led to dietary niacin requirements and food fortification, effectively eliminating pellagra as a public health issue. However, recent research has shown that NAD+ levels naturally decline with age. Unlike pellagra, this decline isn't an outright deficiency, but it raises an important question: What effect does this reduction have on our cells and overall health?

The essential roles of NAD+ in cellular energy and health

NAD+ is indispensable for cellular energy metabolism, driving energy transfer through redox reactions in metabolic pathways like glycolysis and the citric acid cycle, ultimately producing ATP – the cell's primary energy source. Beyond energy production, NAD+

serves as a substrate for enzymes that regulate key cellular processes vital for health and longevity, including sirtuins, PARPs, and CD38. These enzymes rely on NAD+ for metabolic regulation, DNA repair, and cellular signaling.

Together, these roles ensure our cells have the energy and maintenance necessary for life.

The NAD+ pool diminishes with age

NAD+ levels fluctuate, balancing synthesis and breakdown. Aging increases cellular stress, requiring greater demands on NAD+-consuming enzymes to maintain cellular integrity. Meanwhile, the body's ability to synthesize NAD+ diminishes, leading to a gradual decline in NAD+ levels over time.

A major consequence of declining NAD+ levels is the reduced activity of sirtuins, proteins crucial for longevity that regulate metabolism, DNA repair, stress responses, and circadian rhythms. As NAD+ levels drop, sirtuin activity diminishes, impairing these essential functions. (Imai 2016).

Given NAD+'s pivotal role in numerous cellular functions, it's no surprise that its decline is linked to various age-related health issues, such as hypertension, arthritis, cognitive decline, and diabetes. Research highlights the importance of maintaining optimal NAD+ levels for overall health. This has led to growing interest in strategies to combat age-related NAD+ depletion, with NAD+ precursor supplementation being a popular approach.

Supplementing NAD+ precursors to restore NAD+ levels

While NAD+ itself is difficult to supplement directly due to its poor absorption and stability, its precursors, niacin (or nicotinic acid, NA) and nicotinamide (NAM), have been commonly used. However, NA often causes flushing, and NAM's conversion to NAD+ can be limited by feedback inhibition and may even inhibit beneficial sirtuins. The precursors nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN) have gained popularity for their better tolerance and effectiveness in raising NAD+ levels.

NR has been shown to reduce inflammation in adults, increase cerebral NAD+ levels in Parkinson's patients, and improve oxidative stress and physical performance in older adults (Damgaard 2023).

Similarly, NMN has demonstrated benefits in improving physical performance among older adults and athletes, enhancing cardiovascular health in individuals with hypertension, and even lengthening telomeres in men (Benjamin 2024).

While NMN and NR have delivered promising results in animal studies, their effects on humans have proven to be more complex and variable. Individual responses, delivery methods, and other factors have been shown to cause variability. Scientists are exploring personalized approaches and other potential protocols to fully optimize NAD+ boosting strategies, aiming to achieve more consistent and significant health benefits.

Next era NAD+ research: Personalised strategies and innovative solutions

Insights gained from previous studies have opened up new and exciting opportunities for future research questions. Teams in multiple labs are working on more refined approaches to producing more conclusive data and are developing more effective, tailored NAD+ restoring strategies that meet individual needs.

While more people are taking supplements to raise NAD+ levels, it's becoming increasingly apparent that individual responses vary significantly. To address this, NAD+ research is shifting towards personalized approaches. By analyzing genetic and metabolic factors, researchers aim to understand why some individuals respond more strongly than others to different forms of precursor molecules.

One study found that "non-responders" had higher expression levels of NAD+- consuming enzymes.

Additionally, focusing on the change in NAD+ levels, rather than just the dosage, has yielded valuable insights. A recent study demonstrated that the magnitude of NAD+ increase can predict clinical outcomes, providing a potential guide for personalized supplementation (Benjamin 2024).

A major challenge in NAD+ supplementation is the bioavailability of precursors. Scientists are investigating new delivery methods to protect these precursors from breakdown during digestion.

Additionally, clinical studies are examining the efficacy and mechanisms of intravenous NAD+ and precursor administration, which are popular in the wellness industry. Novel precursors with improved stability and tissue-specific targeting are also being explored. By evaluating various administration methods, researchers aim to optimize NAD+ supplementation and enhance its therapeutic benefits.

Wearable technologies and at-home testing kits now offer extensive data on real-world behaviors and health biomarkers, enabling continuous monitoring of individual responses to NAD+ protocols. This creates a powerful synergy between consumers, industry, and academia, providing valuable insights and real-world data. Such collaboration is accelerating scientific understanding and guiding evidence- based wellness practices.

For nearly a century, NAD+ has been recognized as a cornerstone of cellular health. Recent breakthroughs are now unlocking its full potential. As research continues to advance, the promise of NAD+ in enhancing health and longevity is more compelling than ever before.

References

1. Benjamin C, Crews R. Nicotinamide Mononucleotide Supplementation: Understanding Metabolic Variability and Clinical Implications. Metabolites. 2024; 14(6):341. https://doi.org/10.3390/metabo14060341

2. Damgaard MV, Treebak JT. What is really known about the effects of nicotinamide riboside supplementation in humans. Sci Adv. 2023 Jul 21;9(29):eadi4862. https://doi.org/10.1126/sciadv.adi4862. Epub 2023 Jul 21. PMID: 37478182; PMCID: PMC10361580.
3. Imai, Si., Guarente, L. It takes two to tango: NAD+ and sirtuins in aging/longevity control. npj Aging Mech Dis 2, 16017 (2016). https://doi.org/10.1038/npjamd.2016.17

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